



SMMGP Clinical Update - June 2010

Supervised injectable heroin or injectable methadone versus optimised oral methadone as treatment for chronic heroin addicts in England after persistent failure in orthodox treatment (RIOTT): a randomised trial *Strang J, Metrebian N, Lintzeris N, et al. Lancet (2010); 375: 1885-95*

This study screened 301 patients and eventually enrolled 127 to be *randomly* allocated to receive injectable methadone, injectable heroin or oral methadone. Primary outcome was 50% or more negative specimens for street heroin on weekly urinalysis during weeks 14-26. They used mass spectrometry to detect opioid impurities to allow differentiation between prescribed and street heroin.

The '*optimised*' oral methadone regime involved daily doses of 80mg or more with individual titration. There was supervised consumption for at least 3 months then supervision was reduced if clinically appropriate. *Supervised injectable methadone* involved a once daily injected dose with an initial dose calculated from 80% of the oral dose. There was a maximum dose of 200mg daily. The *supervised injectable heroin* group had doses individually titrated and were typically 300-600mg daily. The total daily dose was divided into two, usually equal, doses and the maximum given was 900mg daily. All the injectable treatment doses were self-administered with direct nursing supervision at clinic sites. The clinics were open for two sessions per day – typically 2 hours at 9am and 2pm. There was a patient safety assessment by the nurse 10-20 minutes before and after every dose. There were no takeaway doses of injectable medications.

The results showed patients on injectable heroin were significantly more likely to have achieved the primary outcome than those on oral methadone (72% versus 27%). There was no significant difference in the primary outcome between injectable and oral methadone (39% and 27% respectively). The adverse effects likely to be due to study drugs were one overdose after methadone injection and two overdoses after diamorphine injection. There were no serious adverse effects attributable to oral methadone.

SMMGP comment:

Seldom can the results of a study have been so well known before having been published. Given the other studies that exist it seems clear that injectable heroin is a worthy, evidence-based aspiration and there is a strong moral argument to provide this as a second-line treatment. The use of objective measurements strengthens this position and eases the dilemma of self-reporting in a trial of injectable heroin.

The secondary outcomes are going to be more crucial to convince a wider audience that extends beyond harm-reductionistas and, more importantly, appeals to commissioners. These outcomes are yet to be reported and include use of other illicit drugs, injecting practices, psychosocial and general health, crime and cost-effectiveness. Cost-effectiveness is crucial and the immediate future of IV heroin in the UK may hinge around this issue. It's not one that will be easily ducked in an austere climate of treatment rationalisation.

Decent, therefore expensive, clinical facilities and staffing will be required over and above current practice in many areas. Those that might be tempted to drift back toward injectable methadone as an interim measure will have to consider the lack of a significant difference between injectable and oral methadone that this study highlighted. The cost issue remains a significant one given the level of clinical supervision and support needed. Opiate substitution therapy finds itself threatened politically, ideologically and economically so extending it to injectable therapy may remain an aspiration for the near future.

CUT. A guide to adulterants, bulking agents and other contaminants found in illicit drugs.

Cole C, Jones L, McVeigh J et al. April 2010. John Moores University. Available at Centre of Public Health, JMU (<http://www.cph.org.uk/publications.aspx>)

This is a large report published by John Moores University. It declares itself to be 'an evidence-based overview of the adulterants (here, any substance or organism found in illicit drugs at the

point of purchase other than the active ingredient), their effects on health and the development of messages and other public health interventions to reduce their impact'.

The fundamental issue is that illicit drugs are, by definition, beyond the usual regulatory mechanisms for quality control. They may contain some substances which have been deliberately added to bulk, dilute or even to enhance the effect of the drug. They may also be contaminated with by-products from the manufacturing process.

Overall, the report highlights that there is *less adulteration* than is anecdotally perceived by drug users and dealers. The lurid tales of household cleaning products, brick dust, ground glass and other nasties are often inaccurate and the evidence is that more prosaic substances are often found.

Taking the example of heroin, the review shows that it is most likely to be adulterated with benign substances rather than with products which will cause serious health problems or death. The most commonly identified substances include caffeine, sugars and paracetamol. However, the report also points out that despite these being relatively non-toxic, users still experience serious health problems including infections, cardiovascular problems and poisoning. While nasties like lead or clenbuterol (a decongestant and bronchodilator) have been responsible for some of these it may be that many of the problems are related to bacterial contamination through poor wrapping, storage and transportation as well as the use of unsterile equipment or contaminated diluents.

The report also covers cocaine, methamphetamine, ecstasy and cannabis. There is information on some of the historical context and the study has used forensic analyses, case-studies and surveillance data to give a picture of all the adulterants and contaminants to be found in illicit drugs.

SMMGP comment:

Everyone thinks they know how illicit drugs might be tainted but the authors state: "...reports of the routine adulteration of illicit drugs with 'dangerous' substances are a myth." Anyone working with substance users will have probably have experience of dealing with the consequences of

adulteration and contamination. This report is important because it sets out the facts clearly and objectively.

The illicit nature of much substance use means that there is a whole spectrum of risks to the end user. From simple adulterants such as paracetamol to exotic bacterial infection like anthrax this report gives clarity to the likely issues. It deserves to be widely read and digested.

Factors associated with complicated buprenorphine inductions. Whitley SD, Sohler NL, Kunins HV et al. *Journal of Substance Abuse Treatment* (2010); 39: 51-57

This paper was a retrospective notes review study of 107 patients from an urban community health centre in New York. They defined their primary outcome of 'complicated' induction as anyone who experienced precipitated or protracted withdrawal.

In total, they had 18 patients (16.8%) who had a complicated induction. The factors associated were: recent use of prescribed methadone, recent benzodiazepine use, no prior experience with buprenorphine, and a low initial dose of buprenorphine/naloxone. Their standard office induction regime (56%) involved an assessment using the Clinical Opiate Withdrawal Scale (COWS) to ensure adequate withdrawal before starting treatment. All of the others had home inductions (44%) and did not get the clinical assessment but instead were given a 'home induction kit' which included the medication, additional adjunctive medications (ibuprofen, clonidine and/or loperamide) and an information sheet on the induction.

Self-treatment: Illicit buprenorphine use by opioid-dependent treatment seekers Schuman-Olivier Z, Albanese M, Nelson SE, et al. *Journal of Substance Abuse Treatment* (2010); 39:41-50

This was a two-stage study that looked at illicit buprenorphine use in a cross-sectional analysis of new and existing patients already receiving out-patient treatment. It also had a prospective cohort stage that followed just over three-quarters of the initial participants for 3 months of treatment.

The results of the study suggested that the demand for illicit buprenorphine is driven by people trying to avoid withdrawal and reduce cravings. Those coming into outpatient treatment had a prevalence rate of illicit buprenorphine use of around 61% while those already in treatment had a rate of 32%.

SMMGP comment: This pair of articles explored a couple of facets of buprenorphine treatment in the community. Anyone who has prescribed buprenorphine will have had people who haven't got through the induction. An exploration of some of the factors that make it more complicated is very welcome. The message from the study on complicated buprenorphine inductions is to beware those naive to buprenorphine and those converting from methadone. In addition, those on benzos are more likely to have problems and we should be wary of being over-cautious when deciding initial doses.

Interestingly, the second study also highlighted that the use of illicit buprenorphine rarely represented an attempt to attain euphoria but was more likely to be attempted self-treatment of opioid dependence, pain and depression. It indicates the importance of full assessment to explore further the reasons for using illicit buprenorphine.

Alcohol-use disorders: preventing harmful drinking. NICE. 2010. Available at <http://guidance.nice.org.uk/PH24>

Alcohol-use disorders: diagnosis and clinical management of alcohol-related physical complications. NICE 2010. Available at <http://guidance.nice.org.uk/CG100>

These reports are the latest from the NICE stabes and will eventually make up a trio with 'Alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence' expected in Feb 2011.

The first report makes several recommendations. Some of the public health interventions include: consider introducing a minimum price per unit; reduce the availability of alcohol; and protection of children and young people from alcohol advertising through strengthened regulations.

The clinical orientated advice suggests: more resources for screening and brief interventions;

the prioritisation of alcohol-use disorder as an 'invest to save' measure through commissioning services and making provision for an increase in referrals to structured alcohol treatments; support for children age 10-15 years; screening young people aged 16 and 17 years using validated questionnaires; extended brief interventions with 16 and 17 years old with those drinking hazardously or harmfully; routine screening for adults; brief advice for adults and where needed a session of structured brief advice perhaps using the FRAMES (feedback, responsibility, advice, menu, empathy, self-efficacy) model; and extended brief interventions for adults which might involve motivational interviewing or motivational-enhancement therapy.

The second report moves beyond screening and brief interventions to give guidance on the management of acute alcohol withdrawal, Wernicke's encephalopathy, alcohol-related liver disease and alcohol-related pancreatitis.

When managing acute alcohol withdrawal the guidance emphasises: the importance of local protocols; the use of benzodiazepines and carbamazepine; and the use of assessment tools such as the Clinical Institute Withdrawal Assessment – Alcohol, revised scale (CIWA-Ar) in addition to clinical judgement.

Brief alcohol intervention – where to from here? Challenges remain for research and practice. Nilsen P. *Addiction* 2010; 105: 954-59

This report sets out some of the key brief intervention research findings in the past 30 years and discusses some of the gaps that still exist. One of the first areas it explores is the effectiveness of brief interventions. There are now around 15 systematic reviews and meta-analyses on brief interventions dating back to 1993. Most of them have been in the primary care setting and it is notable that the average duration of a brief intervention in the most recent Cochrane review in 2007 was 20 minutes.

It also explored barriers to brief implementation by health professionals. The research has indicated that some GPs feel they lack the necessary skills, were unsure if the issue came within their responsibilities and had inadequate resources.

SMMGP comment:

The NICE guidance sets out some public health type interventions but there are also some clinical nuggets tucked away here as well. The advice to busy clinicians has to be to consider using the screening tools wherever feasible. We should also be using AUDIT screening tools in 16 and 17 year olds – or at least one of the abbreviated versions. It may not be possible to screen everyone so clinicians may choose to concentrate on higher risk groups – perhaps those that have attended GUM clinics or repeatedly seek emergency contraception.

The brief intervention has enjoyed something of a meteoric rise to fame in the past few years. However, we perhaps have to continue to push and extend its boundaries beyond the perception that it simply means to have a 'bit of a chat' with the patient. The NICE guidance also emphasises this – there is plenty of scope to fine tune and develop brief intervention skills. While NICE suggest that services for extended interventions should expand Nilsen poses the important question, yet to be explored, on just how brief a brief intervention can be and still work.

The paper also makes the point that it is probable that many practitioners already integrate discussions about alcohol into their everyday practice; they just don't refer to them as 'brief interventions'.

Unplanned attempts to quit smoking: a qualitative exploration. *Murray RL, McNeill A, Lewis S, et al. Addiction 2010; 105: 1299-1302*

This study took smokers from a Nottingham randomised controlled trial in 2006 and identified the ones that had given the response in a questionnaire: 'I did not plan the quit attempt in advance; I just did it'. They found 297 participants and ended up with 180 to invite for interview. Only a third responded and ultimately they interviewed 20 people. They used a semi-structured interview, transcribed and then analysed the results to identify themes and sub-themes.

There have been previous studies showing that unplanned quit attempts are actually more likely to succeed. This study showed that many of the quit attempts that are reported in surveys as being 'unplanned' actually have do have an element of planning and delay in them. The study

noted that common reasons for not accessing support were a lack of time, lack of knowledge about available support and, most worryingly, a feeling that the GP would not be receptive to offering support.

SMMGP comment: This article explores some of the elements underpinning smokers who give up without planning in advance – it reaches out to explore the attitudes of the people that wake up in the morning and just decide to quit. Logic might dictate that these people are unreachable and can't be offered any help.

For many of those who are battling against apparently more serious addictions such as heroin or stimulants once a measure of stability is reached it's likely that tobacco may be having the most detrimental effect to their health. It's important for anyone who might be in a position to offer smokers to appreciate that in even those that are apparently unreachable there may still be a window of opportunity to enhance their chances of success.

Hepatitis C virus risk behaviours within the partnerships of young injecting drug users *Hahn JA, Evans JL, Davidson PJ, et al. Addiction 2010; 105: 1254-1264*

This report looked at whether young IDUs (under 30) who perceived that their injecting partner (not necessarily sexual partner) was HCV positive had any association with decreased odds of engaging in receptive needle/syringe sharing (RNS) or other ancillary equipment sharing (AES) with that partner.

The study relied on self-reporting of RNS and AES from 2003 to 2007 in 212 young IDUs (who were HCV antibody negative) in San Francisco. RNS and AES occurred in 23% and 64% respectively of injecting partnerships in the prior month. The odds of engaging in needle/syringe sharing were significantly lower for relationships where the injecting partner was reportedly HCV positive.

SMMGP comment:

This study highlights high levels of sharing in IDUs continue with nearly a quarter of young IDUs sharing needles and syringes and almost two-thirds sharing other equipment at some point in the prior month.

The authors suggest that the findings may infer that young IDUs do engage in some degree of 'risk calculation' in order to avoid infection. However, as they point out, if the HCV status is not known then the risk of sharing was the same as for injecting with someone who is known negative. This might revolve around some kind of user 'don't ask, don't tell' injecting etiquette but it emphasises the critical importance of finding effective harm reduction interventions to reduce sharing given its central role in the spread of blood-borne viruses.

Fluorescent blue lights, injecting drug use and related health risk in public conveniences: Findings from a qualitative study of micro-injecting environments. *Parkin S, Coomber R. Health & Place 2010; 16: 629-637*

This study reports on the findings of an intriguing qualitative study that spoke to IDUs in Plymouth. There are now a number of public toilets that have fluorescent blue lights (FBL). The aim is to discourage IDUs from using public places to inject as the blue colouration makes it difficult to find and use veins.

Over the period Feb-Jun 2008 they recruited current IDUs who had injected in a public setting within the previous month. This provided a sample of 31 individuals. The authors described their average male respondent: typically aged 34, white (British), from the local area, likely to be unemployed, with some experience of homelessness and an average injecting career of 15 years.

All of the 31 respondents were familiar with the blue light phenomenon and could name at least one location with FBL. All but one of them believed they were installed to deter injecting. Over one fifth (7/31) of the sample thought they were a 'good idea' to deter drug use and thus maintain the 'safety' of the public. FBL deterred 13 out of 31 of the sample but only had a partial deterrent effect on 7 out of 31. This group modified the way they used drugs. Some found alternative physical sites – one described going in the neck as those veins could still be found under the FBL. In over one-third (11/31) of the sample there was no deterrent effect. Some of those were attracted to blue light environments as they felt they were less likely to be detected there.

SMMGP comment:

This paper shows that blue lights are only having, at best, a partial effect in deterring IDUs. One common theme running through this paper is that they can increase risky injecting – groin injecting or neck injecting are not particularly affected by the need to see veins but it is harder to detect the difference between venous and arterial blood under FBL.

It's worrying that a range of organisations, from private enterprises to local councils, are implementing these policies. The authors highlight the challenge for health practitioners in convincing those responsible for blue light environments that they are harmful and hazardous to IDUs and that they are actually counter-productive to wider public health.

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